Comparative Homology Modeling and Ligand Docking Study of Human Catechol-O-Methyltransferase for Antiparkinson Drug Design

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Abstract

Catechol-O-methyltransferase (COMT, EC 2.1.1.6) is an S-adenosylmethionine (SAM, AdoMet) dependent methyltransferase, and is related to the functions of the neurotransmitters in various mental processes, such as Parkinson's disease. COMT inhibitors represent a new class of antiparkinson drugs, when they are co-administered with levodopa. Based on x-ray structure of rat COMT (rCOMT), the three dimensional structure of human COMT (hCOMT) wasconstructed by comparative homology modeling using MODELLER. The catalytic site of these two proteins showed subtle differences, but these differences are important to determine the characterization of COMT inhibitor. Ligand docking study is carried out for complex of hCOMT and COMT inhibitors using AutoDock. Among fifteen inhibitors chosen from world patent, nine models wereenergetically favorable. The average value of heavy atomic RMSD was 1.5 Å. Analysis of ligand-protein binding model implies that Arg201 on hCOMT plays important roles in the interactions with COMT inhibitors. This study may give insight to develop new ways of antiparkinson drug.

Reference

1. Zhou, Z. S.; Zhao, G.; Wan, W. "Frontiers of Biotechnology & Pharmaceuticals" 2003, vol.2, 256.